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Transcutaneous
Spectral Blood-Flowmeter

M. P. Fraser

26 March 1970

Prepared under Electronic Systems Division Contract AF 19(628)-5167 by

Lincoln Laboratory

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Lexington, Massachusetts



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TRANSCUTANEOUS SPECTRAL BLOOD-FLOWMETER

M. P. FRASER

Group 68

TECHNICAL NOTE 1970-7

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ABSTRACT

A proposed instrument capable of measuring quantitative blood flow in man is described. The techniques utilized involve no trauma or hazard to the patient and, being transcutaneous, are suitable for clinical use. This report reviews the present status of transcutaneous blood-flowmeters, furnishes a brief tutorial on basic ultrasonic principles and limitations relevant to biological usage, considers the theoretical bases for the proposed techniques, and translates these into a prototype system. Finally, recommendations for initiating a program to devise such an instrument are presented.

Accepted for the Air Force
Franklin C. Hudson
Chief, Lincoln Laboratory Office

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TRANSCUTANEOUS SPECTRAL BLOOD-FLOWMETER

I. INTRODUCTION

Non-traumatic continuous quantitative measurement of blood flow in man can not be achieved with any existing technique. An instrument proposed for clinical use, described in this report, will be capable of performing this measurement in the majority of arteries and veins. Furthermore, it will be able to monitor the non-spatial flow profile in a vessel, the pulsatile flow variation during a cardiac cycle, the vascular lumen-dimension, wall motion, and approximate wall thickness. Additionally, the method is transcutaneous and involves no trauma or hazard to the patient. The instrument utilizes range-gated pulse-Doppler ultrasonic principles and a sophisticated processing system. In use, the instrument probe would be directed, from the patient's skin surface, toward the desired vessel. All vessels in the path of the probe's beam, to the maximum penetration depth of 10 to 15 centimeters, are presented on a display. The desired vessel, after selection, is resolved into appropriate cross-sectional increments by corresponding range gates. The backscatter spectral content of each increment is then determined, utilizing the Doppler effect, and analyzed to yield volume flow. Thus, the measurement is independent of flow profile. The over-all absolute accuracy should approach ± 5 percent.

II. PRESENT STATUS OF DOPPLER TRANSCUTANEOUS BLOOD-FLOWMETERS

The need for non-traumatic transcutaneous flowmeters to continuously monitor blood flow in humans is evidenced by the varied activity in this field. Direct measurement flowmeters under investigation and/or use include hydromechanical, indicator, electromagnetic, thermal, ultrasonic phase or transit-time comparison, and ultrasonic Doppler instruments. The last is the only type promising true non-traumatic reliable measurement capabilities. The others, which are well documented in the literature, will not be discussed further.

A. Source Material

References were compiled utilizing four sources. Index Medicus, a subject-author index to most of the world's biomedical journals, provided the majority of citations. Consideration was given primarily to recent material. The Science Citation Index furnished cross correlation of the material. MEDLARS, the National Library of Medicine's Medical Literature Analysis and Retrieval System, and the Biomedical Communication Network of New York State provided computer-generated bibliographies of current articles and books. The entire search furnished about 200 references, most of which are in English. A bibliography of those most relevant to the present study is appended to this report. The entire bibliography and reprints of all the articles are available in the author's office.

B. CW Doppler Flowmeters

A variety of CW ultrasonic Doppler instruments are available commercially; most sell for several hundred dollars. These instruments are mainly used as an aid in obstetrics by monitoring the presence of the fetal heart beat, blood particle and vessel motion, or any motile structure. Additionally, these units are employed to diagnose peripheral vascular disease. Typically, they transmit a continuous low-power (5 to 50 milliwatts/cm²) ultrasonic beam (2 to 10 MHz) which, when reflected from a moving object and mixed with the transmitted signal, produces a Doppler

frequency in the audio spectrum representing object motion. This signal is reproduced on a loudspeaker. The physician must then utilize past experience, judgment, and a critical ear to interpret the origination and frequency components of the sound. In order to improve on the process, some medical researchers, and at least one commercial manufacturer, have replaced the speakers with strip-chart or electrocardiograph recorders and occasionally preceded these by a finite number of simple filters. The filters separate the response into gross frequency bands. A frequency-to-voltage converter, usually a zero-crossing detector, is also utilized. With these modifications, the instruments now present an indication of the uncalibrated time variation of certain undefined spatial velocity components in the field of the ultrasonic beam. Interpretation of the data still remains partly in the realm of art.

C. Range-Gated Pulse-Doppler Flowmeters

Range-gated pulse-Doppler systems, although relatively complex, are capable of measuring the velocity of a moving object, in the presence of other moving objects, at any desired distance along a beam. Theoretically, a flowmeter based on this principle could monitor the pulsatile blood flow in any specific vessel, to the exclusion of all other vessels. Furthermore, it could be capable of monitoring the flow profile across the vessel, the vascular diameter, wall motion, and possibly wall thickness. The limitations of this method are discussed in Sec. III-H-3. Several researchers are investigating related techniques.

Flaherty and Strauts (1969) have built a simple flowmeter which presents unprocessed Doppler video on an oscilloscope and raw range-gated flow information through a speaker. This flowmeter lacks a sophisticated processing system, furnishes an indication of relative flow only, can not suitably monitor the flow profile across a vessel or distinguish between forward and reverse flow, and does not have the required displays.

The University of Washington maintains an ambitious program in Bio-engineering which includes relevant work in the ultrasonic field. Investigations have included CW Doppler measurements of heart motion, micturition, and blood flow employing limited spectral analysis on some of the resulting waveforms. Research relating to attenuation and thermal effects of ultrasound in specific biological tissues, as well as measurements of the scattering cross section of blood, is being performed. Additionally, Baker and Watkins (1968) have developed a 5-MHz range-gated pulse-Doppler flowmeter similar to the system described above. Although it suffers from the same limitations, the researchers plan to upgrade the processing and display portions of the system.

Peronneau and Leger (1969) at the Broussais Hospital, Paris, have demonstrated a sophisticated flowmeter which promises to be the prototype for much future research. An 8-MHz, 0.5- to 3.0-microsecond transmitted pulse, with an adjustable range gate, resolves blood vessel cross sections sufficiently to permit flow-profile analysis. The present system incorporates only one range gate and processing channel, necessitating the acquisition of data in a time-averaged serial fashion. Two processing schemes have been examined for obtaining flow direction: a servo-controlled local oscillator and a simplified balanced processor. The servo system, however, is basically limited to single-channel operation. In vitro experiments have been performed ascertaining the relationship between velocity, volume flow, spectrum divergence, and linearity as a function of flow profile and viscosity. In vivo experiments, by catheterization and implantation in a dog, have resulted in calibrated velocity profiles indicating cross-sectional

flow reversals during certain portions of the cardiac cycle. Transcutaneous clinical measurements have not been performed and would present certain basic problems, outlined below, which in conversation with Dr. Peronneau had not been given consideration to date. A complex expanded processing system would be required to monitor the entire profile on a real-time basis and to compensate for signal absorption and scattering attributed to the intervening tissues. The angle between the ultrasonic beam and the vessel being monitored would have to be accurately determined to obtain an absolute indication of the blood velocity. Compensation or elimination of signals arising from the transverse components of flow would also be required. Finally, the instantaneous spatial velocity components would have to be converted to volume flow parameters. These propositions are discussed further in Sec. III.

III. ULTRASONICS AND BIOLOGICAL MATERIALS

This section contains a brief tutorial on basic ultrasonic principles relevant to biological usage. Additionally, certain fundamental limitations and problems are explored. The concluding passages outline the theoretical bases for techniques proposed in Sec. IV.

A. Pulse-Doppler Effect

A short burst or pulse of energy transmitted from a source to a moving object will be partially reflected from the object toward a suitably located receiver. A small fraction of the original energy, having experienced a specific shift in frequency, will impinge on the receiver following a unique time lapse. This interval, Δt , representing the total travel time of the energy, is simply

$$\Delta t = \frac{d_s + d_r}{c} \quad , \quad (1)$$

where d_s and d_r are the source-object and object-receiver separation, and c is the velocity of energy propagation in the medium. For most biological materials, such as fat, muscle, or blood fluid, the ultrasonic-energy propagation velocity, c , is approximately that of water: 1.5×10^3 meters per second. Velocity variations between different biological materials are under 10 percent (excluding bone). Although the velocity is relatively independent of the ultrasonic frequency (i.e., non-dispersive), Feldman and Myers (1968) have recently demonstrated some dispersive effects in whole blood. The frequency shift of the returning energy, designated the Doppler frequency, f_d , is related to the source frequency, f_o , by the equation:

$$f_d = \left(\frac{c + v \cos \Theta}{c - v \cos \Phi} - 1 \right) f_o \quad , \quad (2)$$

where Θ is the angle between the object-source vector and the direction of object motion, and Φ is the corresponding angle for the receiver. When the source and receiver are co-spatial, Eq. (2) reduces to the better known approximation:

$$f_d \cong \frac{2 v \cos \Theta}{\lambda} \quad , \quad (3)$$

with the wavelength, λ , defined as c/f_o .

B. Properties of Ultrasonic Waves

Ultrasonic waves consist of the propagation of the particle displacements of a medium at frequencies above the aural range. Each individual particle follows a specific orbit about its own equilibrium position and is not propagated with the wave. The type of orbit determines the type of wave: longitudinal, transverse or shear, Rayleigh or surface, and Lamb.

1. Wave Types

Longitudinal waves travel in all mediums, possess a higher velocity of propagation than other waves, and are easily generated and detected. The particle orbit is parallel to the direction of propagation resulting in alternate plane regions of compression and rarefaction. They are the only waves that a gas or liquid will support and are useful in biological applications. Transverse or shear waves have particle orbits perpendicular to the direction of propagation. Except for very thin film liquids, they can propagate only in solids. Since transverse waves can be polarized in specific directions, they are often used for flaw detection in welds. Rayleigh or surface waves, having elliptical particle orbits, travel over solid surfaces only. Lamb waves, also elliptical, are supported in thin-sheet stock. They behave like electromagnetic waves in a waveguide. Both latter wave types find application in parts testing.

2. Specific Acoustic Impedance

The ratio of the acoustic pressure on a particle of a medium to its velocity is defined as the specific acoustic impedance, Z , of the medium. This impedance can be shown to be the product of the density of the medium, ρ , and the velocity of ultrasonic energy propagation, c , in the medium:

$$Z = \rho c \quad (4)$$

As an example, the longitudinal wave impedances of some representative materials (expressed in $\text{kgm/m}^2\text{-sec}$) are: bone, 2.5×10^6 ; most soft tissue, 1.5×10^6 ; fresh water, 1.4×10^6 ; and air at STP, 413.

3. Interface Effects

When a plane longitudinal wave is incident on a boundary separating two media, reflection and refraction occur. Furthermore, a partial transformation or mode conversion of the longitudinal wave to a transverse, surface, or Lamb wave may occur. The fraction of the wave reflected is determined by the angle of incidence and the ratio of the specific acoustic impedances of the media. For normal incidence, in all media, this fraction is given by

$$\frac{P_R}{P_I} = \left(\frac{Z_2 - Z_1}{Z_2 + Z_1} \right)^2 \quad (5a)$$

where P_R and P_I represent the reflected and incident acoustic power. A 180-degree phase shift occurs in the reflected pressure wave if the impedance of the medium traversed by the incident wave is larger than the second medium; otherwise, no change in phase occurs.

For oblique incidence at non-solid interfaces (which include most biological interfaces), the fraction of the wave reflected is given by

$$\frac{P_R}{P_I} = \left(\frac{Z_2 \cos \theta_i - Z_1 \cos \theta_t}{Z_2 \cos \theta_i + Z_1 \cos \theta_t} \right)^2, \quad (5b)$$

where θ_i and θ_t represent, respectively, the incident and transmitted (refracted) angles between the wave propagation direction and the normal to the interface surface. However, since most biological materials possess similar acoustical parameters, the fraction of the wave reflected in these materials is not a sensitive function of incident (or transmitted) angle, except near the critical angle defined below. The angle of reflection will, of course, change accordingly. For example, at a fat/muscle interface the power in the reflected wave increases by only 3 dB as the incident angle is varied from 0 to 45 degrees.

Methods of analyzing the behavior of obliquely incident waves at solid interfaces are complex. Furthermore, if a mode conversion can be supported in either medium, the fraction of the power contained in other than the longitudinal wave is also a function of the angle of incidence. For normal incidence there is no conversion.

In all cases, refraction of that portion of the wave not reflected, along with mode conversion if supportable, will occur in the second medium. The angles of reflection and refraction are governed, as in optics, by Snell's law:

$$\frac{c}{\sin \psi} = \text{constant}, \quad (6)$$

where ψ represents the angle between the wave propagation direction and the normal to the interface surface. Recognize that the velocity of propagation, c , in any medium will be a function of the wave mode. As in optics, there is a critical angle of incidence at which the longitudinal wave is refracted parallel to the interface. However, there exists a second critical angle, due to the slower propagation velocity of transverse waves, at which the longitudinal wave is transformed, where supportable, and refracted parallel to the interface, resulting in the generation of a surface wave.

Equation (5) predicts that energy passing through air/tissue interfaces will experience a 30-dB loss each way at each interface! Propagation through organs such as lung, stomach, or intestine is thus improbable. Furthermore, additional loss mechanisms are present and are discussed in the following section. Proper coupling of the ultrasonic wave to the skin surface must also be considered.

Multiple reflections, occurring between discrete interfaces, can produce spurious signals interpretable as non-existing structures. Furthermore, the frequency spectrum of any Doppler components will generally be altered by the modified beam geometry. These effects, significant in ultrasonic visualization systems, are negligible in the proposed application. Lateral interfaces may be avoided by appropriate positioning of a relatively thin ultrasonic beam. Axial and unavoidable lateral interface effects can be eliminated by utilizing a narrow range gate. Additionally, the energy of the spurious signals is reduced by each multiple reflection.

C. Energy Loss Mechanisms

The most important energy loss mechanism experienced by an ultrasonic wave traveling through a medium is the conversion of a portion of its energy into heat. This conversion, and resultant wave attenuation, is primarily caused by mechanical interaction between the medium's particles. A secondary loss mechanism can be attributed to the scattering of the ultrasonic energy at discontinuities having dimensions small compared to a wavelength. The wave is

reflected in all directions and the energy loss is related to the volume of scatterers and the fourth power of frequency. This Rayleigh-type scattering is of minor importance as a biological attenuation mechanism as demonstrated by the linear frequency-attenuation relationship discussed below. It is of primary importance, however, as the reflection mechanism in blood, as described in the next section. Diffraction, the bending of a wave around an object, also decreases the energy content of the wave. Its attenuation effect on biological material is negligible.

The attenuation of ultrasonic energy in biological materials has been extensively investigated by several researchers [Dunn (1965), Kossoff, *et al.* (1965), Fry, *et al.* (1962), Carstensen (1960), Schwan (1959), Carstensen, *et al.* (1957), and Goldman, *et al.* (1956)]. Table I lists the mean measured attenuation values, due to all loss mechanisms, for several biological materials. A linear frequency relationship (exponent of 1.0 to 1.3) exists from 1 to 20 MHz except for bone and other calcified materials. For these, the attenuation varies as the square of the frequency to several megahertz and then gradually reverts to the linear dependence. Non-biological liquids and gases exhibit a precise square relationship.

TABLE I
ONE-WAY ATTENUATION OF BIOLOGICAL MATERIALS

<u>Material</u>	<u>Attenuation at 1 MHz (dB/cm)</u>
Fat	0.5
Muscle	1.0
Bone	12-18
Calcified vascular plaques	10-20
Blood	0.16
Water	0.0018
Air, STP	1.4

In addition to the air/tissue interface loss, discussed in the previous section, attenuation of the ultrasonic energy by absorption in most gases is considerable, e.g., 13 dB/cm one way at 3 MHz for air. Furthermore, lung tissue imbedded with air bubbles has 10 dB/cm attenuation at this frequency. The attenuation increases at higher frequencies due to the tissue contribution and at lower frequencies due to energy reradiation induced by bubble pulsation [Dunn (1965)]. Thus, propagation attempts through lung and other gas-filled cavities will probably not succeed. Major bones, with their large attenuation at the higher frequencies, should also be avoided.

D. Ultrasonic Scattering of Blood and Vascular Wall

The scattering properties of biological material, although basic to the proper understanding and application of ultrasonic techniques, have not been thoroughly investigated to date. Reid (1969) and others are presently examining the ultrasonic scattering of whole blood between 4 and 16 MHz. The phenomenon is important because it represents the prime mechanism of energy reflection from the blood. The scattering source appears to be the erythrocytes. Since these are much smaller than the wavelengths under consideration, the scattering should be Rayleigh or fourth-power frequency-dependent. The preliminary measurements, indicating a backscatter cross section related to the projected area of the erythrocytes, confirm this. The cross section, at 5 MHz, for normal blood appears to be 45 dB below the $2/3$ power of the illuminated volume. Furthermore, it is proportional to the hematocrit and not angular dependent — both as expected.

The contributions from platelets, which are much smaller than erythrocytes, and leukocytes, which are few in number, are negligible.

Fragmentary data, obtained in vivo on heart valves, suggest vascular wall backscatter ratios of $-40 \text{ dB m}^2/\text{m}^2$ [Reid (1969)]. This would indicate, utilizing Eq. (5), differences in tissue impedances of only several percent, as expected. The backscatter appears to be frequency-independent and, not being in the Rayleigh region, strongly dependent on incident angle.

E. Biological Effects

The interaction mechanism between ultrasonic energy and biological materials is not completely understood. Although most of the energy is eventually converted to heat, thermal effects are not the fundamental operating factors. Sufficient heat, however, can increase tissue temperatures to lethal levels, especially in the vicinity of bone, which has high ultrasonic absorption properties. Other biological interactions include cavitation (the formation of gas bubbles within the liquid portion of tissue caused by ultrasonic pressure changes), mechanical agitation, alteration of certain biological chemical reactions, and internal cellular modifications. Individual cell necrosis, as well as reversible and irreversible lesions, however, have been experimentally produced without evidence of the presence of any factor discussed above. Pulsed energy levels below 20 watts/cm^2 and continuous levels below 1 watt/cm^2 (for biologically usable wavelengths) appear to be nondestructive by any mechanism, although some cumulative dose effects may occur. Where sensitive tissues, such as ocular or neural fibers, are involved, a more conservative level might be indicated.

F. Ultrasonic Transducers

Ultrasonic energy may be produced by mechanical vibrators, thermal and hydrodynamic devices, magnetostrictive generators, and piezoelectric transducers. The piezoelectrics are capable of practical operation to about 20 MHz; the others are limited to 100 kHz. A new class of transducer, based on the resistive layer thickness of certain semiconductors, operates between several hundred megahertz and a few gigahertz. This class includes diffusion-layer, depletion-layer, and epitaxial transducers.

Piezoelectric transducers, because of their operating wavelengths, are the only class applicable to present biological usage. They are comprised of crystals exhibiting polar or non-symmetrical axes and convert electrical energy to acoustical energy. The applied electric field produces a strain, capable of generating ultrasonic waves, proportional to the field strength. The converse piezoelectric effect, the production of an electric field in the presence of mechanical stress, is equally exhibited. Practical conversion efficiencies range from 10 to 90 percent. Quartz and ceramics (such as barium titanate and lead titanate zirconate) are commonly used materials. Normal operation is in the half-wavelength-thickness mode. Although quartz has lower ultrasonic generation capability than the ceramics, its relative detection output voltage is greater and its non-sintered nature makes it mechanically preferable at the higher frequencies. The ceramics are useful for increased power generation, wider bandwidth (up to 90 percent of the resonant frequency), and where particular characteristics or complex shapes are required. Their major disadvantages include high internal capacitance and very low equivalent radiation resistance. Quartz, conversely, has an exceedingly high radiation resistance. Either extreme imposes severe requirements on the electrical matching networks.

The relationship between a material's piezoelectric parameters and its electrical and ultrasonic performance is theoretically well established. Nevertheless, factors such as practical mounting methods, realizable acoustic loading and damping, attenuation and spurious mode generation in the piezoelectric material, and attainable electrical matching networks introduce sufficient variables to shift optimum transducer design partially toward empirical relationships and craftsmanship. Furthermore, when operated at short pulse lengths, acoustic and electrical damping and matching mechanisms assume primary roles. Short pulse generation may be enhanced by driving the transducer with appropriate time-delayed phase-shifted compensatory signals and the utilization of acoustic impedance-matching transformers.

Many biological applications, due to the physical dimensions and wavelengths involved, restrict transducer operation to the near field or Fresnel region. This is the region extending from the transducer through a series of minimums and maximums in the radiation intensity to the far field or Fraunhofer region. There the radiated beam is fully formed and decreases in energy as the square of the distance from the source. In the near field, the beam deviates in intensity as described, is relatively parallel to the direction of propagation, and exhibits amplitude and phase variation across its wavefronts resulting in the propagation of non-planar waves. Further modification of the wave obviously occurs as the result of interaction with biological material. Additionally, short pulses of energy, due to their shape and finite length, produce more wave aberrations. Clearly, specific analysis of all the factors involved is difficult. Supplementary alterations of the beam pattern may also be produced by modifying the physical shape of the transducer or coupling an ultrasonic lens system, using suitable materials, to the front of the transducer.

G. Beam-Vascular Angle

The angle subtended by the ultrasonic beam and the blood vessel under consideration must be accurately determined in order to obtain quantitative flow information. This angular dependence is indicated by Eq. (2). An approximate determination, useful for initial probe placement, can be obtained from anatomical factors. Further, with the aid of a calibrated probe jig it is possible to ultrasonically locate the exact normal to the vessel by acquiring the Doppler-frequency minimum, theoretically zero. The desired probe angle, for use in blood-velocity measurements, can be set in any plane through the normal. The Doppler frequency can then be maximized by adjusting the angle in the plane orthogonal to the normal. This insures correct beam alignment along the vessel. The probe jig would be invaluable for setting and maintaining the proper angles. Identical portions of the vessel must be utilized for locating the normal and performing the blood-velocity measurement. Thus, the apex of all angles must be taken at the intersection of the normal beam and the vessel, not on the skin surface. This can be done, with an increased probe-jig complexity, since the vessel depth is constantly measured ultrasonically. Due to anatomical factors, however, it may be impractical to locate the normal to certain deep vessels. The use of multistatic techniques suggests an alternative method of angle determination. A minimum of four spatially separated transducers is required. The most basic scheme would utilize a source transducer surrounded by three receiving transducers, all located within a common probe. The angles subtended by the source and receiving beams, corresponding to the transducer orientations, are directly measurable. The angle between the source beam and the blood vessel can then be expressed in terms of these known angles and the three received

Doppler frequencies. The only constraint on the method is that the implied processing be performed for identical blood volumes at coincidental times. Thus, depending on the desired penetration depth, the source-receiving beam angles must be adjusted. This could readily be accomplished by mechanically coupling the receiving transducers and simultaneously adjusting them to obtain maximum Doppler energy return. Unfortunately, the required adjustment negates the advantage of this technique. The use of automatic or electronic scanning, although eliminating this deterrent, would probably result in unjustifiable system complexity.

A non-scanning approach, utilizing the information contained in the amplitude variations of the Doppler return, for example, would be desirable. The ultrasonic energy scattered by the blood, according to the theory developed by Kato (1962), results in a transducer output voltage, E_o , given by

$$E_o = K \sqrt{(aln)(\gamma)(P)} \quad , \quad (7)$$

where K is a constant for any specific condition and includes biological losses and transducer conversion efficiency. The (aln) term represents the total number of erythrocyte scatterers in the illuminated volume. It is composed of the cross-sectional vascular area, a , the total illuminated vessel length, l , and the number of erythrocytes per unit volume, n (related to hematocrit). The erythrocyte's ultrasonic cross section, γ , is directly relatable to the value discussed in Sec. III-D. Finally, P represents the incident power density. It is obviously futile, due to the many biological parameters contributing to the value of K , to attempt utilization of this equation for direct calibration. The length, l , however, varies as the ratio of the ultrasonic beam width to the sine of the beam-vascular angle such that, within limits,

$$E_o \sim \sqrt{\frac{1}{\sin \Theta}} \quad . \quad (8)$$

In order to obtain the value of this angle, the constants in Eq. (7) must be empirically ascertained by setting l at a known value; namely, its minimum ($\Theta = 90$ degrees). Again, the normal to the vessel must be established. Furthermore, different biological material will be penetrated as the beam-vascular angle is changed, resulting in altered values of K and P .

Other techniques, or combinations of those described, may eventually prove useful for angle determination. For the present, it appears that the simple ultrasonic location of the vascular normal is the preferred technique. An additional factor, common to all techniques, is introduced by the refraction of the beam at biological interfaces — particularly at the interface between skin and transducer coupling medium. Proper design and usage can compensate for this effect.

H. Hemodynamics

The characteristics of the flow of blood in biological vessels must be considered for proper flowmeter application. The complexity of the cardiovascular system, including the pulsatile flow variation, precludes the literal utilization of simple hydrodynamic theory. Nevertheless, certain concepts will be useful for a deeper comprehension of succeeding sections.

1. Laminar and Turbulent Flow

A Newtonian fluid (viscosity not a function of shear rate) in a rigid tube of circular cross section will, under steady laminar flow, assume a paraboloid velocity distribution or flow profile.

The average velocity of the fluid will be equal to one half of the axial velocity, and calculation of the volume flow is trivial. If the flow changes from laminar to turbulent, the apparent velocity of the fluid remains practically constant over the cross section. Individual fluid particles, however, assume random velocity vectors. If the true longitudinal average velocity can be measured, the volume flow is self evident. The transition from laminar to turbulent flow is not precise and is a function of the ratio of a fluid's inertial to frictional force. This ratio, known as the Reynolds number, Re , is expressed by

$$Re = \frac{\rho v d}{\mu} \quad , \quad (9)$$

where ρ , v , and μ , respectively, represent the fluid density, velocity, and viscosity. The ratio μ/ρ is designated the kinematic viscosity. The hydraulic depth, d , for circular cross sections, is equal to the diameter. Laminar flow begins to become unstable, under the elementary conditions discussed above, at Reynolds numbers exceeding 2000. Realistic conditions existing in the cardiovascular system include the pulsatile nature of the flow, the non-rigidity of the vessels, disturbances caused by branches and bends, and the non-Newtonian characteristics of blood evident in the smaller vessels. In vessels exceeding 0.5-millimeter diameter, however, blood can be considered a homogeneous Newtonian fluid; thus, suspended erythrocyte behavior approximates whole blood behavior.

2. Vascular Flow Profile

Characteristics of human blood vessels, applicable to the present investigation, are tabulated in Table II. The values are presented as an indication of expected magnitudes and, being collected from diverse sources, are not necessarily precise.

TABLE II
CHARACTERISTICS OF BLOOD VESSELS

<u>Vessel</u>	<u>Mean Diameter (mm)</u>	<u>Pulsatile Diameter Variation (percent)</u>	<u>Approximate Wall Thickness (mm)</u>	<u>Approximate Blood Velocity (cm/sec)</u>
Aorta	20	5-10	1.0	140 (peak)
Common Carotid a.	7-9	3-7	0.6	
Femoral a.	6-7	1-5	0.4	60 (peak)
Brachial a.	3-5		0.3	
Digital a.	0.5-1.0		0.2	
Arterioles	0.01-0.02			1 (mean)
Venules	0.02-0.05			0.2 (mean)
Digital v.				
Brachial v.				
Femoral v.	10-15		0.2	
Internal Jugular v.	15		0.25	5 (mean)
Inferior Vena Cava	30		0.4	5-20

Although venous pulsatile diameter variations are inappreciable, cross-sectional variations of several hundred percent are possible through active dilation and constriction. These have the function of redistributing the blood supply as required to maintain proper pressures and body temperatures. The response times are in the order of minutes. Additionally, the table does not indicate the distribution of blood velocity, or velocity flow profile, across the vascular cross section. This flow profile is a function of the individual person, the vessel involved, and the time of observation. Near the aorta and pulmonary artery, the profile appears to be a flattened paraboloid; in peripheral arteries the paraboloid is distorted by pulsatile phase-lags along the axis; while in the veins the profile approximates the perfect paraboloid expected. Also, recent evidence [Peronneau (1969), Attinger (1964), Montgomery (1964), Wetterer (1962), and McDonald (1960)] suggests that cross-sectional arterial flow reversals, transverse flow, and turbulence occur during certain portions of the cardiac cycle. The production of turbulence in blood vessels depends not only on the Reynolds number, Re , but on the pulsatile velocity spectrum, the vascular geometry, and the characteristics of the vascular wall. It also appears that the vascular cross section, which in some vessels varies 10 percent during a cycle, is elliptical rather than circular. Furthermore, a small change in vascular length occurs during the cycle, creating a longitudinal wall velocity in addition to the expected radial wall velocity. Both these velocities are small compared to the blood velocity.

To obtain quantitative measurements, therefore, the blood vessel must be resolved into a sufficient number of individual elements. The vascular cross section, wall thickness, wall motion, flow, and any corresponding pulsatile variations could then be ascertained. However, the transverse component of flow, which will be present in the received spectrum of any measurement, must first be eliminated. Fortunately, this component varies as the sine of the beam-vascular angle, whereas the longitudinal component, given by Eq. (2), varies as the cosine of the angle. Thus, by measuring the spectrum at two different angles in the plane of the vessel, appropriately weighting and subtracting these from each other, a spectrum results which represents only the longitudinal component of flow. This scheme may be implemented by utilizing two transducers operating at different frequencies. The procedure can be approximated experimentally, for certain flow conditions, with a single transducer, provided that the resultant spectra are synchronized with the cardiac cycle. It may be expedient, though not necessary, to utilize the spectrum obtained at the vascular normal as one of the inputs. Additionally, the probable difference in longitudinal and transverse blood velocity, and the physiological fact that the net average transverse flow must be zero over a longitudinal section large compared to the diameter, may reduce the scope of the problem.

3. Range-Gated Resolution of Flow Profile

The previous section has demonstrated that quantitative measurement of blood velocity involves resolution of the vascular cross section into many independent elements. A range-gated ultrasonic beam, forming a small angle with the vascular normal, accomplishes this in one dimension, along the beam axis. The beam is effectively sliced into unique time sections, and thus measurable distances. If the flow profile is not symmetrical about the vascular axis, as may be the case, a means of resolving the other dimension must be established. This suggests a beam whose width dimensions are small compared to the vascular cross section and which must, consequently, be scanned to cover the desired spatial volume. In principle, this can be accomplished by utilizing several types of steerable narrow beams. Since a relatively large

volume must be scanned in a limited time, steering would probably be performed electronically, utilizing phased-array techniques. Rapid mechanical scanning may also be applicable. The complexity arising from either scheme would not be warranted in an instrument destined for clinical usage. Although medical research requirements might justify such an approach, the use of a catheter-introduced range-gated ultrasonic flowmeter, as developed by Peronneau (1969), should be considered as an alternative.

4. Spectral Resolution of Flow Profile

The cross-sectional average velocity of the blood, as a function of time, can be determined without knowledge of the specific vascular flow profile. The non-spatial instantaneous velocity distribution, if measurable, contains sufficient information. Elementary volumes of erythrocyte carrying blood will backscatter a portion of any incident ultrasonic energy with a resultant Doppler frequency related to the volume's velocity, by Eq. (2), and a magnitude implied by Eq. (7). Thus, the fraction of energy backscattered in any frequency band is directly proportional to that fraction of the total illuminated volume having corresponding velocities. Additional factors which must be considered include the beam-vascular angle, attenuation of ultrasonic energy in the blood, the distribution of erythrocyte scatterers, and transverse velocity components. The beam-vascular angle remains constant during any measurement, and thus can be disregarded. The ultrasonic attenuation in blood, although small, will result in reduced energy return from the far side of the vessel. At 3 MHz, for example, this would amount to a 10 percent maximum energy differential in the larger vessels. Lower frequencies would reduce this accordingly. Variations in erythrocyte distribution would, of course, result in corresponding variations in backscattered energy. Although a controversial subject [Deakin (1969), (1968), Charm (1967), and Jones (1966)], a radial distribution with an outer zone of negligible concentration appears to be presently accepted by medical researchers. This anomaly is mainly apparent in the smaller vessels, under 1 millimeter, and would probably lead to negligible velocity errors in other vessels. A different theory predicts little variation of erythrocyte concentration with radial distance. A range-gated system, such as described in the preceding section, could be used to investigate the erythrocyte distribution in vivo and thus resolve this issue. Finally, transverse velocity components may be resolved as described in Sec. III-H-2. However, by utilizing a beam which is wide compared to the vascular diameter, and employing small beam-vascular angles, the transverse velocity components will be minimized and will probably cancel. This latter approach should be verified experimentally under all expected flow conditions.

The instantaneous velocity distribution of the blood across the vessel, within the limitations outlined, is thus obtainable, though not spatially assignable. Although the flow profile cannot be reconstructed, the known spectral velocity distribution will provide indications of the actual flow nature. Additionally, certain mathematical parameters, such as the average instantaneous velocity, are calculable. For example, given spectral power density, $P(f)$, vs frequency, f , as available from the received instantaneous distribution, the average frequency, \bar{f} , is

$$\bar{f} = \frac{\int f P(f) df}{\int P(f) df} \quad (10)$$

On a discrete basis, this equation reduces to

$$\bar{f} = \frac{\Delta f \sum_{n=-N}^N (n - \frac{1}{2}) P(n)}{\sum_{n=-N}^N P(n)} , \quad n \neq 0 , \quad (11)$$

where a total of $2N$ contiguous filters of corresponding bandwidth Δf , and corresponding center frequency $N\Delta f/2$, are utilized. The conversion between average frequency and average velocity is then trivial. A specific implementation of this approach is presented in Sec. IV-D.

5. Determination of Vascular Dimensions and Flow

In order to determine the vascular flow rate, the average instantaneous blood velocity must be combined with the average instantaneous vascular cross-sectional area. Additionally, knowledge of vascular dimensions would be valuable for clinical diagnoses. A possible method of obtaining this information utilizes aspects of the pulse-Doppler technique described previously. Signals arising from adjoining vessels or biological structures may be excluded by bounding the desired vessel with a movable variable-width range gate. The vascular depth and approximate diameter are thus established. Determination of precise vascular cross-sectional dimensions, and their pulsatile variation, may be accomplished by utilizing a contiguous series of fine-grain range gates positioned around the vascular walls. The minimum resolvable vascular dimension is directly related to the width of these gates and the generated ultrasonic pulse. The width of the pulse, in turn, sets a practical lower limit on the ultrasonic frequency. Thus, short pulses of high frequency are required for proper resolution. It may be desirable, under certain conditions, to switch transducer operation to a higher harmonic for this measurement. For the special case of two major targets located within the minimum resolvable dimension, as defined above, the actual resolvable dimension is smaller and related to the width of the gate, the rise and fall time of the ultrasonic pulse, and the system noise. In practice, this would allow improved resolution of such major reflections, occurring at surfaces normal to the beam, as the near and far sides of the vascular walls. Additionally, the semi-fluid motile tissue surrounding the vessel may affect the measurement of wall thickness and should be considered.

Although most vessels appear to be nearly circular in cross section, several – such as the pulmonary arteries – exhibit definite elliptical cross sections. In order to determine their shape, several measurements must be obtained at different aspect angles. Furthermore, all individual measurements must be performed simultaneously or synchronized with the cardiac cycle. As a practical matter, where possible, the measurements should be made at the vascular normal. Calculation of the actual instantaneous vascular flow must, again, utilize simultaneous or cardiac-synchronized velocity and cross-sectional information.

Finally, as shown in Eq. (7) and experimentally verified by Kato (1964), the internal cross-sectional area of any specific vessel is proportional to the total power backscattered at all Doppler frequencies. This relationship might prove useful for monitoring relative cross-sectional variations during the cardiac cycle; it could not be applied on an absolute basis for reasons similar to those discussed in Sec. III-G.

I. Spectral Spreading of Backscatter

Ultrasonic energy impinging on moving erythrocytes will be backscattered at a frequency implied by Eq. (2). Several mechanisms, however, cause a spectral spreading of this energy;

these include Brownian mobility of the erythrocytes, undesired transducer motion, and diverse angular position of the erythrocytes in a beam of finite width. The Brownian or constant thermal mobility of the erythrocytes will generate a symmetrical spectrum centered around the expected Doppler return. For ultrasonic frequencies in the megahertz region, this spectrum has a negligible width of less than one hertz.

Unrestricted transducer-probe motion, relative to the blood vessel, could result in excessive broadening of the received spectrum. An appropriately secured transducer probe utilizing straps, tape, or a suction apparatus, can be expected to maintain its position to fractions of a millimeter with peak frequency components of several hertz. This would result in a maximum spectral broadening of several tens of hertz.

Finally, individual scatterers illuminated by a beam of finite width will backscatter energy at frequencies corresponding to their angular position in the beam. This phenomenon has been investigated by Green (1964) in the far field and Albright (1969) in the near field. The width of the resultant scattered spectrum appears to vary as the ratio of transverse scatterer velocity to beam cross section in the near field (reciprocal of beam angle in the far field). Thus, for probable blood velocities and nominal transducer dimensions, a spectral spread of 10 to 100 hertz, being a function of the specific parameters involved, would result.

The spectrum produced by the simultaneous action of all the phenomena described is the convolution of the individual spectra. Although the resultant spectral width will probably be less than 100 Hz, the phenomena involved warrant further consideration because of their significance and their diverse treatment in the existing literature.

IV. PROTOTYPE FLOWMETER

System considerations for a prototype flowmeter, based on the spectral resolution of flow profile outlined in Sec. III-H-4, are presented in this section. It has been assumed that a penetration of 15 centimeters, representing 10 centimeters depth at nominal beam-vascular angles, is desirable. Additionally, resolution comparable to the minimum considered vascular cross section (for the spectral analysis processing) and the minimum considered wall thickness (for the cross section and wall parameter processing) is required. These considerations, along with the relationships implied by the equations in Sec. III and the biological constraints expounded previously, serve to delineate the principal system parameters listed in Table III. The determination of certain parameters not discussed previously is explained in succeeding paragraphs.

TABLE III
PROTOTYPE FLOWMETER PARAMETERS

Operating frequency	3.0 MHz
Pulse width	2.0 μ sec
Pulse repetition rate	8.0 kHz
Ultrasonic beam cross section	1.0 cm ²
Peak ultrasonic output power	1.0 watt
Average ultrasonic output power	16 mW
Maximum expected Doppler frequency	4.0 kHz
Penetration depth utilizing processor	15 cm

A block diagram of the prototype flowmeter is shown in Fig. 1; the average flow network portion is detailed in Fig. 2. The solid lined section represents the spectral resolution portion of the system. The dashed lined section represents the cross section and wall parameter determination portion, probably not implemented initially. Although analog processing is indicated, system complexity may justify the use of digital processing. Preliminary system flow data and further study will help resolve this question. Also, initial processing will probably be accomplished by utilizing existing Laboratory computer facilities, thus maintaining maximum flexibility at a minimum cost. The following paragraphs describe individual parts of the system. Figure 3 is a representation of expected outputs on the system displays.

A. Transducer and Generating Circuitry

The Stable Oscillator, shown in Fig. 1, produces a continuous-wave low-power output at 3.0 MHz. Since the backscattered frequency will be mixed with the generated frequency, the latter should be stable, to a fraction of the minimum expected Doppler frequency, over the signal comparison time. A short-term (1 msec) frequency stability of 1 part in 10^7 is therefore adequate. The long-term stability is not critical. The Buffer Amplifier increases the signal power to the level required to produce 1 watt of ultrasonic energy at the transducer, probably in the order of 10 watts, allowing for losses in the electric and acoustic matching networks.

The Pulse Modulator and Transducer Compensator modulates the incoming continuous-wave signal with a 2- μ sec pulse followed by a time-delayed phase-shifted compensatory signal. This latter signal helps to reduce undesired transducer ringing. The basic repetition rate, determined by the Timing Circuit, is synchronized with the Stable Oscillator in order to obtain coherent output pulses. Since the maximum expected Doppler return is 4 kHz, the minimum pulse repetition frequency required to avoid ambiguous velocity components is 8 kHz. Unfortunately, signals scattered from beyond 10 cm will be ambiguous in range with signals scattered from the first 5 cm. This ambiguity may be avoided by suitable transducer positioning. There will be no ambiguous signals when operating up to 10 cm, since these are automatically eliminated by the range-compensated gain adjustment discussed in Sec. IV-C. Additionally, there will be a blind zone extending for several millimeters near 10 cm penetration. This zone, however, may be relocated by adjusting the transducer position or the pulse repetition frequency.

The Switching and Limiting Circuitry, consisting of fast diode switches, connects the transducer to the generator or to the receiver at the appropriate time. The limiting portions of the circuit protect the receiver from large ambiguous signals and accidental overloading. With proper diode operation, the increased receiver noise figure will just equal the circuit insertion loss - less than 1 dB.

The transducer design will require additional study to obtain optimum performance. The initial design will probably utilize a 1-cm² ceramic material with appropriate acoustic impedance matching. The resultant beam will allow illumination of moderate-size vessels with reasonable precision. A transducer with a wider beam, 2 or 3 cm², would be useful for illuminating larger vessels and investigating the cancellation of transverse velocity components described in Secs. III-H-2 and III-H-4. The peak ultrasonic power could then be increased accordingly. Implementation of the transverse velocity processor is not planned initially. The mechanical probe jig (Sec. III-G) and the electric Impedance Matching Network (Sec. III-F) also require further study.



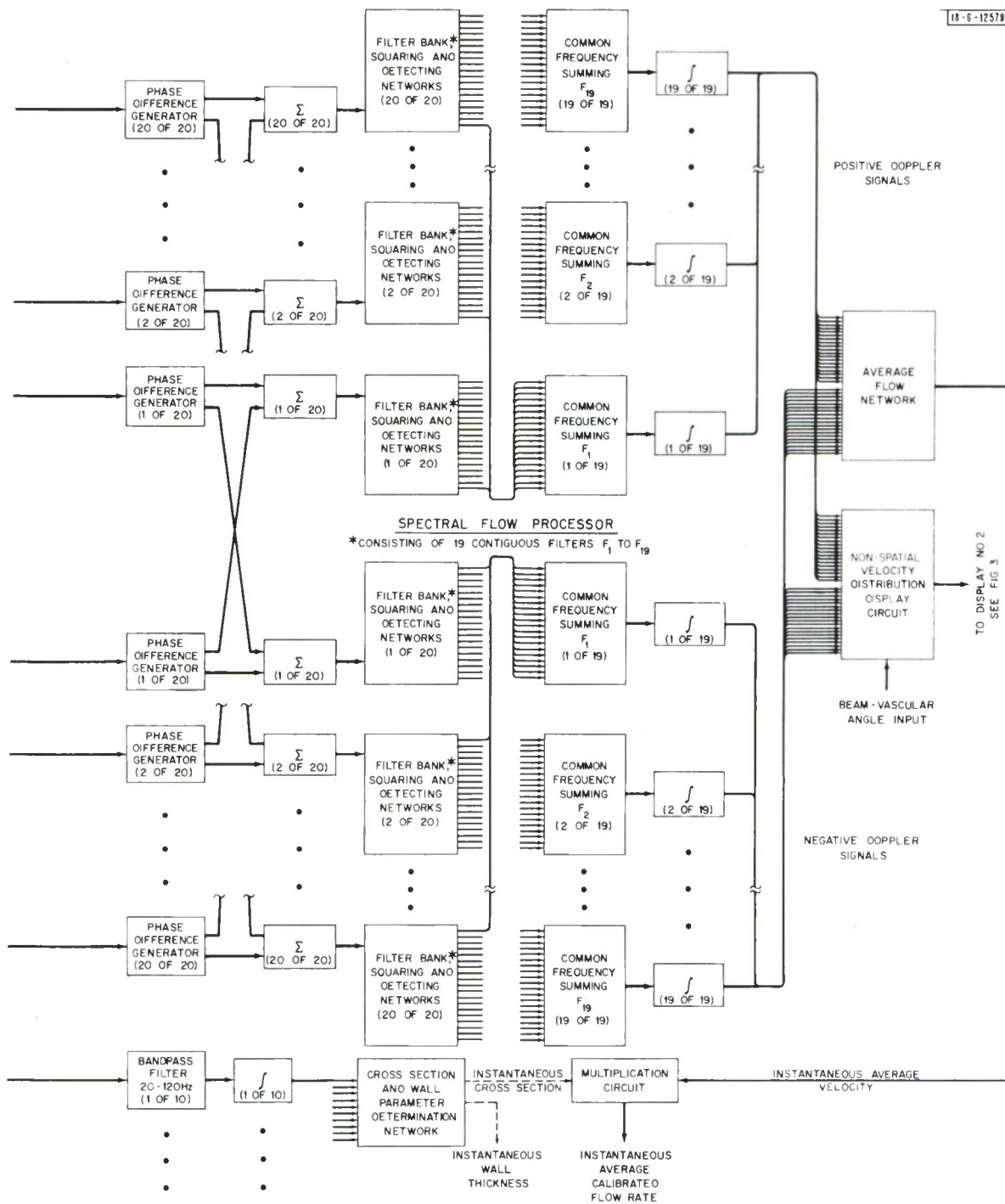


Fig. 1. Continued.

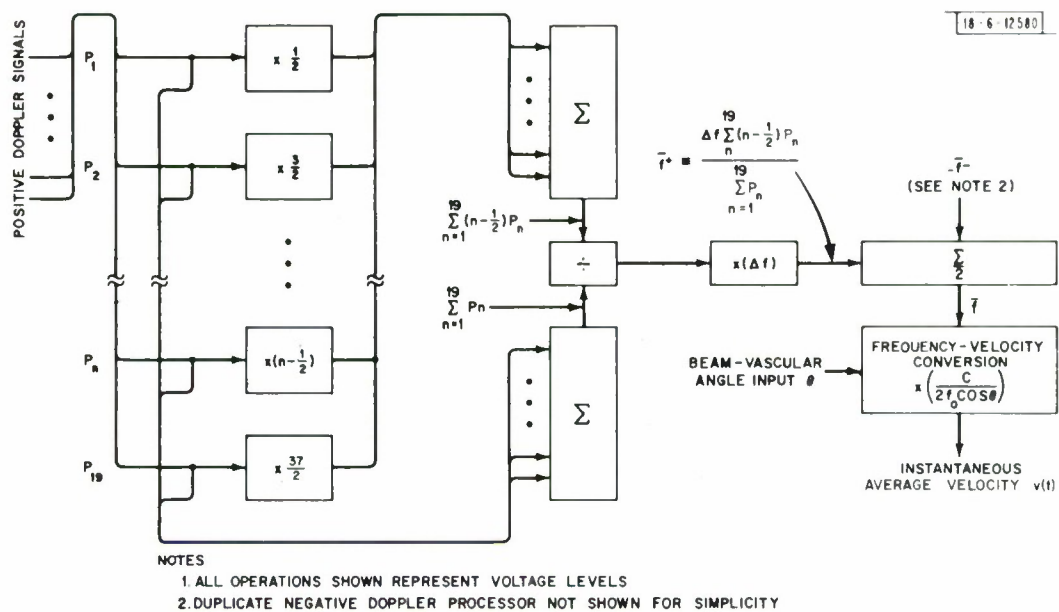


Fig. 2. Average flow network.

B. Biological Signal Modification

The acoustic signal emanating from the transducer, having a peak intensity of 1 watt/cm^2 , passes through a thin layer of an acoustical coupling gel and into the skin surface. Due to differences in acoustical impedances, a negligible portion of the signal is reflected. Differences in propagation velocity, however (expected to be under 5 percent), will result in beam refractions of 2 or 3 degrees, depending on the probe-skin angle. Appropriate calibration of the probe jig could negate any resultant errors.

The 3-MHz acoustic signal, having traversed up to 15 cm of soft tissue (assumed to consist of 70 percent muscle and 30 percent fat), will have been attenuated 38 dB due to absorption and an estimated 6 dB due to beam scattering and diffraction. There is no inverse square-law dependence since the entire beam is in the near field. Thus, a peak power density of -44 dBW/cm^2 exists at the maximum desired penetration depth. This power is backscattered from the blood, which has an apparent cross section at 3 MHz of 53 dB below the $2/3$ power of the illuminated volume. For a typical vessel, 5 to 6 millimeters in diameter (0.4 cm^2 projected area per centimeter length), this yields a backscatter power level of -101 dBW . The signal arrives at the transducer, after an additional 44-dB attenuation loss, at a power level of -145 dBW . A further loss, estimated at 8 dB, is experienced in the transducer and matching networks, mainly in the latter. Finally, the signal passes through the Switching and Limiting Circuitry, with a 1-dB loss, into the receiver.

C. Receiver and Mixer

On entering the receiver, the desired signal and those arising from adjoining vessels and biological structures pass through the Coarse Range Gate, adjustable in both range penetration and width. An oscilloscope presents a display (Fig. 3, Display 1) of the Raw Bipolar Video, from succeeding stages, vs Penetration Depth (appropriately calibrated as a function of beam-vascular angle). The desired signal, with its characteristic Doppler returns, can now be selected by adjusting the Coarse Range Gate. An audio representation of the Doppler return is also available on an auxiliary speaker. Proper setting of the Coarse Range Gate, besides eliminating undesired signals, permits readout of the approximate vascular dimensions. The minimum practical gate width is equivalent to the generated pulse width and the obtainable resolution. Thus, vascular dimensions may be ascertained within 1 or 2 mm. Signal-to-noise ratio degradation will limit the display to penetration depths somewhat less than 15 cm. At maximum penetrations, the Coarse Range Gate must be adjusted by observing the output of the Filter Banks, probably a more demanding procedure.

A low-noise RF Amplifier increases the signal levels for further processing. Signals emanating from peripheral vessels and biological structures may be 100 dB above the minimum design signals. Therefore, in order to reduce the system dynamic-range requirement, a Range-Compensated Gain Adjustment is included in the RF Amplifier. This adjustment is automatically provided by the penetration setting of the Coarse Range Gate. The gain would be set at a minimum of 25 dB and increased approximately 6 dB per centimeter to a maximum of 110 dB, resulting in mean output levels of -45 dBW . The reduced dynamic-range requirement, now related only to variations in biological returns at similar ranges (including provision for spectral resolution of the blood velocity), is 30 dB maximum. This implied response linearity across the band is applicable to the entire system. Additionally, in order to properly resolve the received

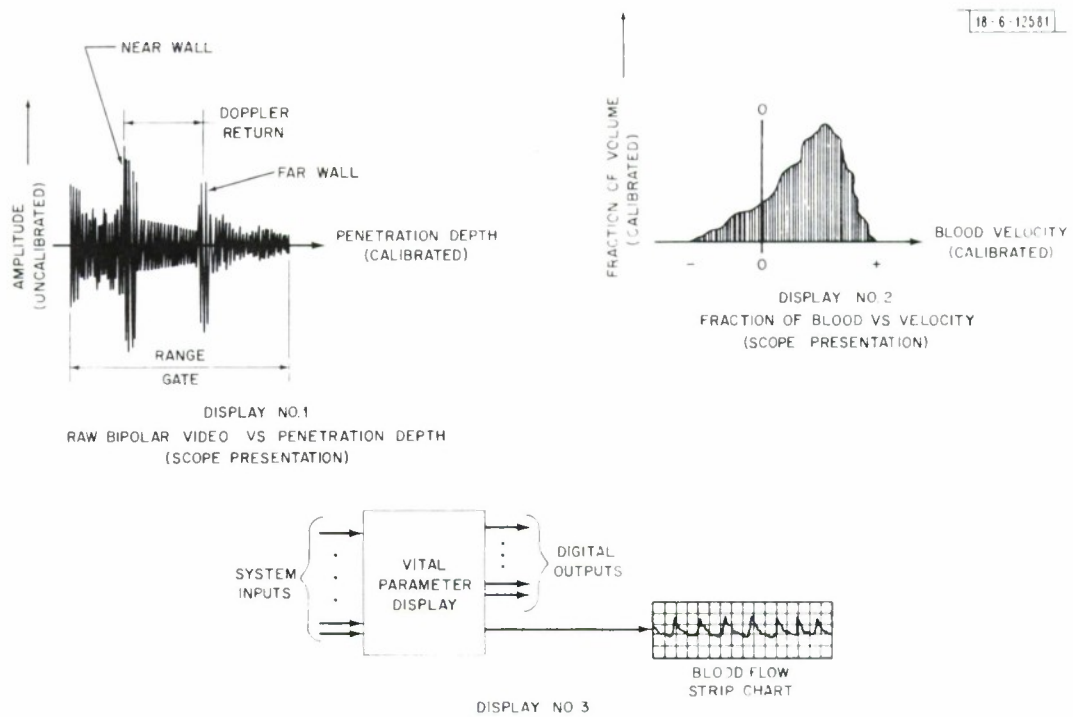


Fig. 3. Display representations.

signals corresponding to the 2- μ sec generated pulse, the RF Amplifier bandwidth must be a minimum of 1 MHz. To permit experimental resolution of vascular dimensions to fractions of a pulse width, as explained in Sec. III-H-5, the prototype RF Amplifier should have greater bandwidth capability, perhaps a total of 5 MHz. The nominal available signal-to-noise ratio, for 1-MHz bandwidth, will be 15 dB at penetrations to 10 cm. An equivalent signal-to-noise ratio exists at the Filter Banks, described in Sec. IV-D, to almost 15 cm due to their relatively narrow bandwidth. The exact signal-to-noise ratio will be a function of the spectral power density distribution.

The In-Phase Power Splitter provides the two identical equi-phased signals required by the Balanced Processor whose individual components are described below. This processor permits determination of the sign of all Doppler shifts; thus, the direction of the velocity components. The two Balanced Mixers, which operate as coherent bipolar detectors, produce outputs on two channels which are in phase quadrature with each other. Their reference signals, split in quadrature phase by the Quadrature Hybrid, are obtained from the Stable Oscillator. Undesired intermodulation products are eliminated by the Bandpass Filters. Their 500-kHz upper cutoff is high enough to maintain the required resolution; their 20-Hz lower cutoff, which could be adjustable, eliminates signals from stationary and non-active structures. Finally, each output is amplified and divided into 22 separate signals by the Video Distribution Amplifiers. One signal from each channel enters a Summing Network for presentation on the display and speaker described previously. A 4-kHz Low-Pass Filter eliminates undesired signals from the speaker. One additional signal from each channel is available for experimental computer processing. It is planned that initial processing will be accomplished in this manner; thus, none of the succeeding circuitry will be required immediately. The remaining 20 identical signals from each channel would be available for further processing, as described below, when needed.

D. Spectral Flow Processor

The processing required to convert the bipolar quadrature-video signals into a non-spatial blood-velocity distribution may be accomplished by several techniques, both analog and digital. The analog technique described below, and indicated in the remaining portion of Fig. 1, is presented as one possible solution to this proposition. Determination of the optimum technique will require further study and collection of data related to blood flow.

Twenty Video Distribution Amplifier signals per channel are available for further processing. This number is chosen such that the largest blood vessels under consideration can be adequately resolved, though not spatially (see Secs. III-H-3 and III-H-4), throughout their entire cross section. Thus, twenty contiguous 2- μ sec resolution increments, representing a 3-cm range extent, adequately encompass most vessels at all nominal beam-vascular angles. The actual number of signals actively processed at any time, typically less than 20 pairs, will be automatically determined by the Coarse Range Gate setting. Each active signal is sampled in the Sample-and-Hold circuits once every pulse repetition period and stored until the next sampling time. The sampling time of contiguous Sample-and-Hold circuits is staggered by 2 μ sec, as determined by the Timing Circuit. Thus, a low-frequency waveform is constructed from each Sample-and-Hold circuit representing the Doppler response in the corresponding range increment. Each pair of outputs is then combined such that an indication of the relative input phase, corresponding to the sign of the equivalent Doppler frequency, is obtained. This is accomplished by utilizing

wideband Phase Difference Generators which produce two outputs differing in phase by 90 degrees. These outputs are cross-coupled and summed, in 20 respective pairs, producing corresponding pairs of signals representing positive and negative Doppler frequencies. Each signal is then directed to a separate Filter Bank for power spectral density estimation.

There are twenty Filter Banks per channel, each containing 19 individual contiguous bandwidth filters covering the desired frequency range. The filter parameters discussed below are calculated for arterial flow. A 4000-Hz upper limit was chosen, corresponding to the maximum expected arterial blood velocity, typically 140 cm/sec, and nominal beam-vascular angles. A 200-Hz lower limit excludes wall motion from the measurement and may be decreased as warranted. The optimum filter bandwidth, as derived below, is near 200 Hz. Smaller filter bandwidths result in better frequency resolution but require longer signal processing times. Thus, if the spectrum changes rapidly it will not be properly sensed by a narrower filter. The maximum arterial blood velocity gradients, which occur in portions of the human aorta, appear to be in the order of 1000 cm/sec², corresponding to the initial 100 msec of systolic flow. This velocity gradient will produce a Doppler frequency gradient of 40,000 Hz/sec (cycles/sec²). Since the approximate response time of a filter is inversely proportional to its bandwidth, the maximum Doppler shift which it can accommodate in this time approaches its bandwidth. The optimum filter bandwidth is therefore equal to the square root of the Doppler frequency gradient, 200 Hz. This corresponds to a nominal velocity resolution of 7 cm/sec per range increment, depending on the beam-vascular angle.

Individual filter outputs are squared and detected to provide power reference levels and summed with their common-frequency filter outputs from all other range-incremented Filter Banks. The 19 resultant outputs per channel are then smoothed by individual integrators to improve the accuracy of the spectral estimation. Although the integration time should be as large as possible, time variations in the signal spectrum set a practical limit on the allowable processing time. Thus, assuming an available processing time of 10 msec (representing one-tenth of the systolic percussion wave), an integration time of 5 msec is indicated, the other 5 msec corresponding to the 200-Hz filter response time. The trade-off between frequency resolution (filter bandwidth) and accuracy or stability of the estimation (integration time) should be rigorously analyzed. Most venous flow, with correspondingly slower velocities, smaller gradients, and lack of rapid pulsatile wall motion, would imply longer integration times, smaller filter bandwidths, and reduced frequency extent, perhaps by a factor of 7.

Alternatively, by sampling each quadrature video channel only once per pulse repetition frequency, rather than 20 times, the circuit complexity could be greatly reduced with a corresponding decrease in estimation accuracy. The required number of Sample-and-Hold circuits, Phase Difference Generators, and Filter Banks would be reduced by a factor of 20.

The 38 outputs of the Balanced Processor, representing the relative power level in each corresponding Doppler frequency band, are processed further in the Non-Spatial Velocity Distribution Display Circuit and the Average Flow Network. The Display Circuit, an oscilloscope interface, contains vertical scale-compensation and horizontal sweep-stepping circuitry. The display, an example of which is shown in Fig. 3, Display 2, presents a modified spectral density plot; namely, the instantaneous non-spatial blood velocity vs the fraction of the illuminated volume (and thus the vascular cross-sectional area) possessing corresponding velocities. For clarity, it might be considered the non-spatial vascular flow profile.

Finally, the Average Flow Network, detailed in Fig. 2, converts the incoming signals, which are equivalent to the respective Doppler frequencies, to the instantaneous cross-sectional average blood velocity. The conversion, which is straightforward, entails a strict implementation of Eqs. (3) and (11). When this resultant velocity is combined with the instantaneous vascular cross section, obtained from the Cross-Section Processor (or approximately from the Coarse Range Gate), the average calibrated blood flow as a function of time is secured.

The Vital Parameter Display, depicted in Fig. 3, accepts inputs from various parts of the prototype system and presents the data in a digital format. Some of the possible outputs include maximum, minimum, and average values of blood volume flow, blood velocity, vascular cross section, wall thickness and velocity, cardiac rate, and of course the desired temporal volume flow, the latter probably on a paper strip chart.

E. Cross-Section Processor

The cross section and wall parameter determination portion of the prototype system is represented by the dashed section of Fig. 1. Wall backscatter signals, for typical vessels 5 to 6 mm in diameter, are expected to be 10 dB above corresponding blood backscatter signals; namely, -91 dBW at 15 cm penetration. This is a consequence of a $-40 \text{ dB m}^2/\text{m}^2$ backscatter ratio and a -10 dB ratio of wall area normal to the beam to total beam illumination area. The required Video Amplifier gain is therefore somewhat less than the corresponding spectrum processor RF Amplifier gain. To permit resolution of vascular dimensions to 0.3 mm, corresponding to 20 percent of the pulse width or approximately one cycle of RF (see Sec. III-H-5), the required amplifier bandwidth is 5 MHz - thus, the nomenclature Video. Since the signs of the Doppler shifts are not needed, a single-ended processor fed by a Balanced Mixer, a 2.5-MHz Bandpass Filter, and a 10-channel Video Distribution Amplifier is utilized.

In order to completely observe the thicker vascular walls and their accompanying displacements, five range triggers per wall, contiguously spaced at 0.3 mm (equivalent to $0.4 \mu\text{sec}$), are generated by the Timing Circuit and supplied to corresponding Sample-and-Hold Circuits. One set of triggers is automatically positioned at the beginning of the Coarse Range Gate; the other, before the end. To obtain arterial dimensions, the Sample-and-Hold outputs are filtered by a 20- to 120-Hz Bandpass Filter which passes only Doppler frequencies corresponding to typical arterial wall velocities of 0.5 to 3 cm/sec. The minimum equivalent filter signal-to-noise ratio is 16 dB. After integration, the signals enter the Cross Section and Wall Parameter Determination Network. This network, containing timing logic, determines which range increments possess appropriate Doppler wall signals and computes the instantaneous wall thicknesses and vascular cross section. Corrections are made for the probable 5 to 10 percent difference between vascular wall and blood propagation velocity. Determination of venous dimensions will require sensing very low Doppler frequencies which, under certain conditions, will approach zero and be unmeasurable. However, this lack of motion will permit satisfactory non-Doppler measurements to be obtained by utilizing the Coarse Range Gate.

If desired, available Doppler signals could be processed for spectral density content by circuitry similar to that used in the Spectral Flow Processor. Additionally, if better range resolution is required, the system frequency could be increased with a corresponding decrease in resultant penetration depth.

V. RECOMMENDED PROGRAM

The clinical need for a quantitative blood-flowmeter is well established in the literature. Furthermore, the feasibility of developing such a flowmeter, utilizing pulse-Doppler spectral-processing techniques, has been demonstrated in this report. It is recommended that a program be initiated to design, construct, and analyze the operation of the prototype flowmeter, described in Sec. IV, and to collect sufficient in vitro and in vivo flow data to optimize future designs. The early and continuous cooperation of medical staff personnel, preferably associated with cooperating hospitals, is a prerequisite of any successful effort. The medical staff will be invaluable for redefining program objectives, making continuing value judgments on measurements, data analysis, and proposed effort redirection, supplying facilities and materials for in vivo testing, and finally, securing future acceptance of these techniques by the medical community at large.

A. Minimal Effort

A minimal effort, which could be accomplished in one year, involves the participation of one full-time and three part-time staff members, one full-time senior programmer, and at least one full-time engineering assistant and/or technician. Represented disciplines should include antenna and propagation theory (transducer design), mechanical engineering (probe jig), signal processing (digital and analog analysis), computer programming, general circuit theory and hardware implementation ability, and of course an appreciation of the related medical aspects.

The basic program includes the construction of the prototype flowmeter, the collection and analysis of in vitro and in vivo flow data, and the investigation of certain related problem areas. Specifically, after any medical staff program redefinition, the prototype flowmeter design will be rigorously optimized on a theoretical basis. The flowmeter will then be constructed less the processing circuitry, that task being delegated to the Laboratory computer facilities. Initial in vitro testing will involve basic flow experiments utilizing blood substitutes (such as milk, dextrin solution, starch suspension, silicon fluid, etc.) in rigid and flexible plastic tubing. These experiments will determine proper flowmeter performance under different tubing sizes, flow rates, and flow profile conditions (including turbulence). Eventually, whole blood will replace the substitutes because the acoustical behavior of these differs somewhat from blood. Finally, in vivo tests will be performed at cooperating hospitals. All data will be recorded on magnetic tape and analyzed by the Laboratory's IBM 360 facilities. Concurrently, a preliminary study of optimum flowmeter parameters and signal processing techniques will be undertaken utilizing the resultant data. Additional areas of investigation will include resolution of the transverse velocity components, the effect of differential blood attenuation and variation in erythrocyte distribution on the spectral density, relative and absolute cross-section measurement techniques, and spectral content of vascular-wall backscatter. The problem of beam-vascular angle determination will receive major emphasis. The measurement of this angle represents the primary limitation on absolute flow accuracy. Secondary factors include some of the items discussed above and the specific processing methods implemented (e.g., filter granularity and integration times). It is expected that an over-all absolute accuracy approaching ± 5 percent will be possible.

B. Expanded Effort

An expanded and relatively complete program would require the full-time participation of four staff members and appropriate ancillary personnel for a period of 18 months. It would

involve the completion of all tasks outlined in the minimal effort and include the construction and initial testing of an optimum real-time processing system. Additionally, it would permit necessary experimentation relating to variation of ultrasonic propagation velocity in biological materials, blood dispersion and backscatter cross section, spectral spreading, and other supplementary subjects. Furthermore, the sophisticated pulse-Doppler and processing equipment available (both off- and on-line) could be utilized for introductory studies of related Doppler effects, such as micturition, swallowing, and the observation of motile structures, as well as non-Doppler effects, such as tissue differentiation potentialities for tumor detection.

ACKNOWLEDGMENT

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GLOSSARY OF MEDICAL TERMS

CATHETER	A tube used for transporting fluids or small instruments within body cavities
CARDIOVASCULAR	Pertaining to the heart and blood vessels
ERYTHROCYTE	Red Blood corpuscle
FETAL	Pertaining to the developing unborn offspring after the second month
HEMATOCRIT	The volume percentage of erythrocytes in whole blood
HEMODYNAMICS	The study of the movements of blood in the circulation
IN VITRO	Within a test tube
IN VIVO	Within the living body
LESION	Any discontinuity of tissue or loss of function of a part
LEUKOCYTE	White blood corpuscle
LUMEN	The space within a tube or tubular organ
MICTURITION	The passage of urine
MOTILE	Able to move spontaneously
NECROSIS	Death of tissue
PLAQUE	Any patch or flat area
PLATELET	A formed element of blood concerned with coagulation and other functions
TRANSCUTANEOUS	Performed through the intact skin
TRAUMA	A physical or emotional wound
VASCULAR	Pertaining to or composed of blood vessels

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13. ABSTRACT A proposed instrument capable of measuring quantitative blood flow in man is described. The techniques utilized involve no trauma or hazard to the patient and, being transcutaneous, are suitable for clinical use. This report reviews the present status of transcutaneous blood-flowmeters, furnishes a brief tutorial on basic ultrasonic principles and limitations relevant to biological usage, considers the theoretical bases for the proposed techniques, and translates these into a prototype system. Finally, recommendations for initiating a program to devise such an instrument are presented.		
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